

WHAT IS CLAIMED IS:

1. An isolated human, murine, or yeast sentrin polypeptide that inhibits TNF receptor or Fas/APO-induced apoptosis.

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2. The polypeptide according to claim 1, wherein said sentrin polypeptide is a sentrin-1 polypeptide.

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3. The polypeptide according to claim 2, wherein said sentrin-1 polypeptide comprises an amino acid sequence having at least 10 contiguous amino acids of SEQ ID NO:2.

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4. The polypeptide according to claim 3, wherein said sentrin-1 polypeptide comprises the amino acid sequence of SEQ ID NO:2.

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5. A purified nucleic acid segment encoding a human, murine, or yeast sentrin polypeptide.

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6. The nucleic acid segment of claim 5, wherein said nucleic acid segment encodes a human sentrin-1 polypeptide.

7. The nucleic acid segment of claim 6, further defined as encoding a polypeptide comprising an amino acid sequence having at least 10 contiguous amino acids of SEQ ID NO:2.

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8. The nucleic acid segment of claim 7, further defined as encoding a polypeptide comprising the amino acid sequence of SEQ ID NO:2.

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9. The nucleic acid segment of claim 5, further defined as an RNA segment.

10 10. A nucleic acid segment comprising the nucleic acid sequence of SEQ ID NO:1, or the complement thereof, or a sequence which hybridizes to the sequence of SEQ ID NO:1, under conditions of high stringency.

15 11. The nucleic acid segment of claim 10, comprising an isolated sentrin gene.

12. The nucleic acid segment of claim 11, comprising an isolated human, murine, or yeast sentrin gene.

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13. The nucleic acid segment of claim 12, wherein said segment encodes an amino acid sequence comprising at least about 10 contiguous amino acid residues from SEQ ID NO:2.

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14. The nucleic acid segment of claim 10, wherein said sentrin gene encodes a polypeptide of from about 15 to about 45 amino acids in length.

15. The nucleic acid segment of claim 10, wherein said sentrin gene encodes a polypeptide of from about 46 to about 75 amino acids in length.

5 16. The nucleic acid segment of claim 10, wherein said sentrin gene encodes a polypeptide of from about 76 to about 100 amino acids in length.

10 17. The nucleic acid segment of claim 10, wherein said sentrin gene encodes a polypeptide of about 101 amino acids in length.

15 18. The nucleic acid segment of claim 10, further comprising a recombinant vector.

19. The nucleic acid segment of claim 10, wherein said nucleic acid is operatively linked to a promotor, said promoter expressing said nucleic acid segment.

20 20. A recombinant host cell comprising the nucleic acid segment of claim 10.

21. The recombinant host cell of claim 20, further defined as a prokaryotic cell.

25 22. The recombinant host cell of claim 21, further defined as a bacterial cell.

23. The recombinant host cell of claim 20, further defined as an eukaryotic cell.

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24. The recombinant host cell of claim 23, further defined as a yeast cell or an animal cell.

5 25. The recombinant host cell of claim 24, wherein said cell is a mammalian cell.

10 26. The recombinant host cell of claim 20, wherein said nucleic acid segment is introduced into the cell by means of a recombinant vector.

15 27. The recombinant host cell of claim 20, wherein said host cell expresses said nucleic acid segment to produce a sentrin polypeptide.

20 28. The recombinant host cell of claim 27, wherein said sentrin polypeptide comprises an amino acid sequence having at least 10 contiguous amino acid residues from SEQ ID NO:2.

25 29. A method of using a nucleic acid segment that encodes an isolated mammalian or yeast sentrin polypeptide, comprising the steps of:

30 (a) preparing a recombinant vector in which a mammalian or yeast sentrin polypeptide-encoding nucleic acid segment is positioned under the control of a promoter;

(b) introducing said recombinant vector into a host cell;

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(c) culturing said host cell under conditions effective to allow expression of the encoded polypeptide; and

(d) collecting said expressed sentrin polypeptide.

30. A nucleic acid characterized as:

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(a) an isolated nucleic acid segment comprising a sequence region that consists of at least 14 contiguous nucleotides that have the same sequence as, or are complementary to, 14 contiguous nucleotides of SEQ ID NO:1; or

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(b) an isolated nucleic acid segment of from 14 to about 10,000 nucleotides in length that hybridizes to the nucleic acid segment of SEQ ID NO:1; or the complement thereof, under standard hybridization conditions.

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31. The nucleic acid segment of claim 30, further defined as comprising a sequence region that consists of at least 14 contiguous nucleotides that have the same sequence as, or are complementary to, 14 contiguous nucleotides of SEQ ID NO:1.

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32. The nucleic acid segment of claim 30, further defined as comprising a nucleic acid segment of from 14 to about 10,000 nucleotides in length that hybridizes to the nucleic acid segment of SEQ ID NO:1, or the complement thereof, under standard hybridization conditions.

33. The nucleic acid segment of claim 32, wherein the segment comprises a sequence region of at least about 20 nucleotides; or wherein the segment is about 20 nucleotides in length.

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34. The nucleic acid segment of claim 33, wherein the segment comprises a sequence region of at least about 30 nucleotides; or wherein the segment is about 30 nucleotides in length.

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35. The nucleic acid segment of claim 34, wherein the segment comprises a sequence region of at least about 40 nucleotides; or wherein the segment is about 40 nucleotides in length.

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36. The nucleic acid segment of claim 35, wherein the segment comprises a sequence region of at least about 50 nucleotides; or wherein the segment is about 50 nucleotides in length.

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37. The nucleic acid segment of claim 36, wherein the segment comprises a sequence region of at least about 100 nucleotides; or wherein the segment is about 100 nucleotides in length.

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38. The nucleic acid segment of claim 37, wherein the segment comprises a sequence region of at least about 200 nucleotides; or wherein the segment is about 200 nucleotides in length.

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39. The nucleic acid segment of claim 38, wherein the segment comprises a sequence region of at least about 300 nucleotides; or wherein the segment is about 300 nucleotides in length.

5 40. The nucleic acid segment of claim 39, wherein the segment comprises the sequence of SEQ ID NO:1.

10 41. The nucleic acid segment of claim 31, wherein the segment is up to about 10,000 basepairs in length.

15 42. The nucleic acid segment of claim 41, wherein the segment is up to about 5,000 basepairs in length.

20 43. The nucleic acid segment of claim 42, wherein the segment is up to about 4,000 basepairs in length.

44. The nucleic acid segment of claim 43, wherein the segment is up to about 3,000 basepairs in length.

25 45. The nucleic acid segment of claim 44, wherein the segment is up to about 2000 basepairs in length.

46. A method for detecting a nucleic acid sequence encoding a sentrin polypeptide, comprising the steps of:

5 (a) obtaining sample nucleic acids suspected of encoding a sentrin polypeptide;

10 (b) contacting said sample nucleic acids with an isolated nucleic acid segment encoding said sentrin polypeptide under conditions effective to allow hybridization of substantially complementary nucleic acids; and

15 (c) detecting the hybridized complementary nucleic acids thus formed.

47. The method of claim 46, wherein the sample nucleic acids contacted are located within a cell.

48. The method of claim 46, wherein the sample nucleic acids are separated from a cell prior to contact.

20 49. The method of claim 46, wherein the isolated sentrin polypeptide-encoding nucleic acid segment comprises a detectable label and the hybridized complementary nucleic acids are detected by detecting said label.

25 50. A nucleic acid detection kit comprising, in suitable container means, an isolated sentrin nucleic acid segment and a detection reagent.

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51. The nucleic acid detection kit of claim 50, wherein the detection reagent is a detectable label that is linked to said sentrin nucleic acid segment.

5 52. The nucleic acid detection kit of claim 50, further comprising one or more restriction enzymes.

10 53. A composition, free from total cells, comprising a polypeptide having a primary sequence which comprises at least about 10 contiguous amino acid residues from SEQ ID NO:2.

15 54. The composition of claim 53, comprising a polypeptide having a primary sequence which comprises at least about 15 to about 20 contiguous amino acid residues from SEQ ID NO:2.

20 55. The composition of claim 53, comprising a polypeptide having a primary sequence which comprises at least about 21 to about 30 contiguous amino acid residues from SEQ ID NO:2.

25 56. The composition of claim 53, comprising a polypeptide having a primary sequence which comprises at least about 31 to about 40 contiguous amino acid residues from SEQ ID NO:2.

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57. The composition of claim 53, wherein said polypeptide comprises a recombinant polypeptide, a fusion polypeptide, or a polypeptide having an amino acid sequence mutated in one or more amino acid residues compared to native sentrin.

5 58. A purified antibody that binds to a mammalian or yeast sentrin polypeptide, wherein said antibody also binds to the polypeptide of SEQ ID NO:2.

10 59. The antibody of claim 58, wherein said antibody is linked to a detectable label.

15 60. The antibody of claim 60, wherein said antibody is linked to a biotin label, a radioactive label, a fluorogenic label, a nuclear magnetic spin resonance label, or an enzyme that generates a colored product upon contact with a chromogenic substrate.

20 61. The antibody of claim 60, wherein said antibody is linked to an alkaline phosphatase, hydrogen peroxidase or glucose oxidase enzyme.

25 62. A transgenic animal having incorporated into its genome a transgene that encodes a mammalian or yeast sentrin polypeptide.

30 63. A method of detecting a ubiquitin conjugating enzyme polypeptide, comprising contacting said polypeptide with an amount of a sentrin-1 polypeptide and composition effective to bind said ubiquitin conjugating enzyme polypeptide, and detecting the complexes so bound.

5 64. A method of detecting a PML polypeptide, comprising contacting said polypeptide with an amount of a sentrin-1 polypeptide composition effective to bind said PML polypeptide, and detecting the complexes so bound.

10 65. A composition comprising an amount of a polypeptide according to claim 53 effective to inhibit TNFR- or Fas/APO-1-induced apoptosis.

15 66. A method for detecting a sentrin polypeptide, comprising the steps of:

(a) obtaining a sample suspected of containing a sentrin polypeptide;

(b) contacting said sample with a first antibody that specifically binds to a sentrin polypeptide under conditions effective to form an immune complex; and

20 (c) detecting the immune complex so formed.

25 67. A method of inhibiting or preventing TNFR- or Fas/Apo-1 induced apoptosis comprising administering to a mammal a pharmaceutical composition comprising an amount of a sentrin polypeptide composition effective to inhibit or prevent said apoptosis.

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68. A method of inhibiting or modulating sentrin polypeptide function in a mammal, comprising administering to said mammal a composition comprising an antibody that specifically binds a sentrin polypeptide.

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69. A method of determining the aggressiveness of a tumor, comprising determining the amount of a sentrin polypeptide produced by a cell and comparing the amount so produced with a normal cell wherein overexpression of the protein is indicative of the aggressiveness of said tumor.

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70. A method of producing cell-death in a tumor cell, said method comprising contacting said tumor cell with a composition effective to prevent sentrinization in said cell.

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71. The method of claim 70, wherein said sentrinization is prevented by blocking the interaction of sentrin and Ubc9.

72. The method of claim 70, wherein said composition comprises a C-terminal peptide fragment of sentrin.

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